

What is claimed is:

1. An isolated nucleic acid molecule which encodes a HICP protein, comprising a nucleotide sequence at least about 60% homologous to a nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3 or a complement thereof.
2. The isolated nucleic acid molecule of claim 1 comprising the nucleotide sequence of SEQ ID NO:1 or a complement thereof.
3. The isolated nucleic acid molecule of claim 2, further comprising nucleotides 1-883 of SEQ ID NO:1.
4. The isolated nucleic acid molecule of claim 2, further comprising nucleotides 1534-1708 of SEQ ID NO:1.
5. The isolated nucleic acid molecule of claim 1 comprising the nucleotide sequence of SEQ ID NO:3 or a complement thereof.
6. The isolated nucleic acid molecule of claim 5, further comprising nucleotides 1-635 of SEQ ID NO:3.
7. The isolated nucleic acid molecule of claim 1 which specifically detects a HICP nucleic acid molecule relative to a nucleic acid molecule encoding a non-HICP protein.
8. An isolated nucleic acid molecule comprising a nucleotide sequence encoding a protein which comprises an amino acid sequence at least about 60% homologous to the amino acid sequence of SEQ ID NO:2.
9. The isolated nucleic acid molecule of claim 8 comprising a nucleotide sequence encoding a protein which comprises the amino acid sequence of SEQ ID NO:2.
10. An isolated nucleic acid molecule encoding a HICP protein, comprising a nucleotide sequence which hybridizes under stringent hybridization conditions to a nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO:1 or SEQ ID NO:3.

~~11.~~ An isolated nucleic acid molecule comprising a nucleotide sequence which hybridizes under stringent hybridization conditions to a nucleic acid molecule comprising nucleotides 1-883 of SEQ ID NO:1.

5 ~~12.~~ An isolated nucleic acid molecule at least 500 nucleotides in length which hybridizes under stringent hybridization conditions to a nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO:1 or SEQ ID NO:3.

10 ~~13.~~ An isolated nucleic acid molecule which is at least about 60% homologous to a nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3 or a complement thereof, and encodes a polypeptide which has at least one of the following activities:

- 15 i) it can modulate cell proliferation;
 ii) it can modulate a growth factor signaling pathway;
 iii) it can modulate the activity of CTGF or PDGF; or
 iv) it can modulate a heparin-induced response in a heparin-responsive cell.

14. The isolated nucleic acid molecule of claim 13 comprising the nucleotide sequence of SEQ ID NO:1 or a complement thereof.

20 15. The isolated nucleic acid molecule of claim 13 comprising the nucleotide sequence of SEQ ID NO:3 or a complement thereof.

25 16. An isolated nucleic acid molecule which is antisense to the nucleic acid molecule of any of claims 1, 9, 11 or 13.

17. A vector comprising the nucleic acid molecule of any of claims 1, 8, 10, or 13.

30 18. The vector of claim 17, which is a recombinant expression vector.

19. A host cell containing the vector of claim 18.

20. A method for producing HICP protein comprising culturing the host cell of claim 19 in a suitable medium until HICP protein is produced.

35 21. The method of claim 20, further comprising isolating HICP protein from the medium or the host cell.

22. A nonhuman transgenic animal which contains cells carrying a transgene encoding HICP protein.

23. A nonhuman homologous recombinant animal which contains cells having an altered HICP gene.

24. An isolated HICP protein comprising an amino acid sequence at least about 60% homologous to the amino acid sequence of SEQ ID NO:2.

25. An isolated HICP protein which is encoded by a nucleic acid molecule comprising a nucleotide sequence at least about 60% homologous to a nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, or a complement thereof.

26. An isolated HICP protein which is encoded by a nucleic acid molecule comprising a nucleotide sequence which hybridizes under stringent hybridization conditions to a nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO:1 or SEQ ID NO:3.

27. An isolated HICP protein which is sufficiently homologous to the amino acid sequence of SEQ ID NO:2 and retains HICP biological activity.

28. The isolated protein of claim 27 comprising an amino acid sequence at least about 60% homologous to an amino acid sequence of SEQ ID NO:2.

29. An isolated HICP protein comprising an amino acid sequence at least about 60% homologous to the amino acid sequence of SEQ ID NO:2 and which has at least one of the following biological activities:

- i) it can modulate cell proliferation;
- ii) it can modulate a growth factor signaling pathway;
- iii) it can modulate the activity of CTGF or PDGF;
- iv) it can modulate a heparin-induced response in a heparin-responsive cell;
- v) it can modulate cell motility; or
- vi) it can modulate extracellular matrix production.

30. The isolated protein of any of claims 24-29, comprising an N-terminal IGFBP motif.

31. The isolated protein of any of claims 24-29, comprising a VWC motif.

32. The isolated protein of any of claims 24-29, comprising a TSP1 motif.
- 5 NO:2. ~~33.~~ An isolated protein comprising the amino acid sequence of SEQ ID
- ~~34.~~ A fusion protein comprising a HICP polypeptide operatively linked to a non-HICP polypeptide.
- 10 ~~35.~~ An antibody that specifically binds HICP.
36. The antibody of claim 35, which is monoclonal.
37. The antibody of claim 36, which is labeled with a detectable substance.
- 15 38. A pharmaceutical composition comprising the protein of any one of claims 24-29, or 34, and a pharmaceutically acceptable carrier.
- 20 39. A pharmaceutical composition comprising the antibody of claim 35 and a pharmaceutically acceptable carrier.
- 25 ~~40.~~ A method for modulating a cell-associated activity comprising contacting a cell with an agent which modulates HICP protein activity or HICP nucleic acid expression such that the cell-associated activity is altered relative to the cell-associated activity of the cell in the absence of the agent.
41. The method of claim 40, wherein the agent stimulates a HICP protein activity or expression.
- 30 42. The method of claim 40, wherein the agent inhibits a HICP protein activity or expression.
43. The method of claim 42, wherein the agent is an antisense HICP nucleic acid molecule.
- 35 44. The method of claim 42, wherein the agent is an antibody that specifically binds to HICP.

45. The method of claim 40, wherein the cell is present within a subject and the agent is administered to the subject.

5 ~~46.~~ A method for treating a subject having a disorder characterized by aberrant HICP protein activity or nucleic acid expression comprising administering to the subject a HICP modulator such that treatment of the subject occurs.

47. The method of claim 46 wherein the HICP modulator is a nucleic acid molecule encoding a HICP protein.

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~~48.~~ A method for detecting the presence of HICP activity in a biological sample comprising contacting a biological sample with an agent capable of detecting an indicator of HICP activity such that the presence of HICP activity is detected in the biological sample.

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49. The method of claim 48, wherein the agent detects HICP mRNA.

50. The method of claim 49, wherein the agent is a labeled nucleic acid probe capable of hybridizing to HICP mRNA.

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51. The method of claim 48, wherein the agent detects HICP protein.

52. The method of claim 48, wherein the agent is a labeled antibody capable of specifically binding to HICP protein.

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Sup H1 ~~53.~~ A method for treating a disorder characterized by aberrant cell proliferation by administering to a subject having the disorder a HICP agent which alters cell proliferation relative to cell proliferation in the absence of the agent.

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54. The method of claim 53, wherein the HICP agent is a HICP protein or portion thereof.

55. The method of claim 53, wherein the HICP agent is a nucleotide encoding a HICP protein.

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56. The method of claim 53, wherein the disorder is a cardiovascular disorder.

57. The method of claim 53, wherein the disorder is a fibrotic disorder.

58. A diagnostic assay for identifying a genetic alteration in a cell sample, the presence or absence of the genetic alteration characterized by at least one of (i) aberrant modification or mutation of a gene encoding a HICP protein, and (ii) mis-regulation of said gene or (iii) aberrant post-translational modification of a HICP protein.

59. The assay of claim 58, wherein detecting said alteration includes:

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- a. providing a reagent comprising a diagnostic probe of claim 11 or 12;
 - b. combining said reagent with nucleic acid of said cell sample; and
 - c. detecting, by hybridization of said probe to said cellular nucleic acid, the existence of at least one of a deletion of one or more nucleotides from said gene, an addition of one or more nucleotides to said gene, a substitution of one or more nucleotides of said gene, a gross chromosomal rearrangement of all or a portion of said gene, a gross alteration in the level of an mRNA transcript of said gene, or a non-wild type splicing pattern of an mRNA transcript of said gene.
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60. The assay of claim 58, wherein detecting said alteration includes:

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- a. providing a reagent comprising two diagnostic probes;
 - b. combining said reagent with nucleic acid of said cell sample; and
 - c. detecting, by amplification or lack of amplification of said cellular nucleic acid, the absence or existence of said alteration.

25 61. A method for isolating a heparin specie which has antiproliferative activity comprising:

- a. contacting a HICP affinity reagent with a composition containing heparin species; and
 - b. isolating the heparin specie which binds to the HICP affinity reagent to thereby obtain the heparin specie which has antiproliferative activity.
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